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| 09/780,041 | 02/09/2001 | Ronald Klein | UF-10293 | 8442 |

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| EXAMINER | |
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| FALK, ANNE MARIE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/780,041 | KLEIN ET AL. | |
| | Examiner | Art Unit | |
| | Anne-Marie Falk, Ph.D. | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *May 17,*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *23-28,30-35 and 39-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) - is/are allowed.

6)☒ Claim(s) *23-28,30-35 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 August 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The amendment filed May 17, 2004 has been entered. Claims 23, 25, 27, 30, 31, 34, and 35 have been amended. Claims 29, 36, 37, and 38 have been cancelled. Claims 39-41 have been newly added. The remarks filed April 22, 2004 (hereinafter referred to as "the response") are considered herein.

Accordingly, Claims 23-28, 30-35, and 39-41 are pending in the instant application.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 9, 2002 (Paper No. 12) has been entered.

### *Drawings*

**New corrected drawings are required** in this application because Figures 3G-3K appear as black rectangles and do not show the features referred to in the specification. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

The drawings are objected to under 37 CFR 1.83(a) because Figures 3G-3K fail to show the features as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). A proposed drawing

correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

At page 8, paragraph 1 of the response, Applicants state that they are deleting Figures 3G-3K. On the contrary, corrected drawings deleting Figures 3G-3K have not been submitted. Figures 3G-3K appear on the same page with Figures 3C-3F.

### *Claim Objections*

Claim 32 is objected to because it covers non-elected subject matter. The elected invention is drawn to a method for producing a non-human animal model by transferring a gene encoding an aberrant form of tau, using somatic gene transfer techniques, a non-human animal comprising in its somatic cells a gene encoding an aberrant form of tau, and a method for inducing behavioral changes by somatic administration of a gene encoding an aberrant form of tau. The elected invention does not cover the use of animals with other genetic modifications.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34 and 35 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims read on a human being comprising the gene recited in the claims. Human beings are non-statutory subject matter.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### *Written Description*

Claims 23-28 and 30-35 stand rejected and Claims 39-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are referred to the final guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, Number 4, pp. 1099-1111 (also available at www.uspto.gov).

The claims are directed to a method for producing a model of a neurodegenerative disease by somatically transferring a viral vector comprising a gene encoding an aberrant form of atau protein into brain tissue of a living rat or mouse under conditions which result in the expression of said gene, wherein expression of said gene results in a neuropathology corresponding to said neurodegenerative disease. Claims 34 and 35 are directed to compositions comprising a gene encoding an aberrant tau protein in a vector construct. These claims encompass animals comprising the gene, but the specification fails to describe the great variety of animals covered by these claims. Furthermore, with regard to the method claims, the specification fails to describe the genus of rats and mice exhibiting "a neuropathology ... corresponding to [a] neurodegenerative disease." The specification only describes genetically-modified rats that exhibit some features similar to those seen in Alzheimer's Disease (AD). Additionally, the Declaration of Dr. Klein demonstrates that somatic genetic modification of mice also results in a phenotype similar to that seen in the rats. However, the claims are directed to a large genus of rats and mice exhibiting a wide variety of phenotypes, namely any kind of neuropathology corresponding to a

neurodegenerative disease. However, the specification does not describe rats and mice exhibiting any phenotype other than a neurofibrillary pathology as disclosed in the specification (p. 14, lines 15-19). Furthermore, this phenotype does not constitute a **model** of the specific diseases recited in Claim 24, as it does not model the complex phenotypic features of those diseases. The claims broadly recite that the rat or mouse has "a neuropathology ... corresponding to said neurodegenerative disease." The term "neurodegenerative disease" refers to a wide variety of disparate diseases, but the phenotype described in the specification does not "correspond to" any of them. For example, amyloid plaques are a major hallmark of AD, but the rats disclosed in the specification do not exhibit amyloid plaques. For the reasons discussed in the interview of 5/10/04, it is unclear if neurofibrillary tangles (NFT) are formed in the rats because it is unclear where the "filaments" referred to in the specification are located (see the Interview Summary dated 5/12/04). In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In this case, since phenotype cannot be predicted for a genetically-modified rat or mouse for the reasons discussed herein below and no working examples describe a genetically-modified rat or mouse of the type claimed, other than a rat or mouse having the specific pathologic phenotype disclosed at p. 14, lines 15-19, no other genetically-modified rats or mice having a neuropathology corresponding to a neurodegenerative disease have been described by their complete structure. Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In this case, since phenotype cannot be predicted from the gene being introduced, no identifying characteristics are provided for genetically-modified rats or mice exhibiting another neuropathology. This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the genus of genetically-modified rats and mice of the type recited in the claims at the time the application was filed; rather only rats and mice having the specific pathologic phenotype disclosed in the specification were described at

the time of filing. Thus, it is concluded that the written description requirement is not satisfied for the claimed genus.

At page 8, paragraph 3 of the response, Applicants assert that the amendments to Claims 23 and 30 obviate this rejection. Since the claims continue to cover the use of rats and mice that have (i) a wide variety of phenotypes not described in the specification, (ii) a wide variety of tau isoforms and (iii) a wide variety of tau mutations, the amendments clearly do not obviate this rejection.

***Enablement***

Claims 23-28 and 30-35 stand rejected and Claims 39-41 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record and for further reasons as discussed herein, because the specification, while being enabling for (i) a method for producing a mouse or rat genetically modified by administration of a viral vector encoding a mutant form of human tau comprising the P301L mutation, wherein the mouse or rat exhibits a neurofibrillary pathology as disclosed in the specification; (ii) a method for inducing behavioral changes in a mouse or rat by administration of a viral vector encoding a mutant form of human tau comprising the P301L mutation; and (iii) a viral vector adapted for *in vivo* expression in a mouse or rat brain tissue, said vector comprising a gene encoding a mutant form of human tau comprising the P301L mutation, does not reasonably provide enablement for the broad scope of animals produced by transferring a gene encoding an aberrant form of tau as claimed nor the methods for producing said animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses rats that have been genetically modified by administration of an AAV vector encoding a mutant form of human tau (designated P301L tau in the specification). At page 14, lines 15-19, the specification discloses that the rats exhibit abnormal accumulation of tau in neuron cell

bodies and dendrites, filaments immunoreactive for hyperphosphorylated tau, neuritic immunoreactivity for several antibodies that recognized neurofibrillary tangles in Alzheimer's and FTDP-17, and a dramatic increase of reactive astrogliosis.

The specification fails to provide an enabling disclosure for the preparation of the full scope of genetically-modified rats and mice as claimed, exhibiting an appropriate phenotype, other than genetically-modified rats and mice having the phenotype mentioned in the preceding paragraph, because the phenotype of a genetically-modified rat or mouse cannot be predicted.

The specification fails to provide an enabling disclosure for the preparation of genetically-modified rats and mice harboring a gene encoding an aberrant form of tau because the guidance offered in the specification is not sufficient to teach one of skill in the art how to prepare the genetically-modified rats and mice exhibiting a phenotype other than the phenotype disclosed in the specification. The mere capability to perform gene transfer in any given species is not enabling for the genetically-modified rats and mice recited in the claims nor for methods of producing them because the desired phenotype cannot be predictably achieved by simply introducing a construct as recited in the claims (i.e., a viral vector comprising a gene encoding an aberrant form of tau protein). While gene transfer techniques are well-developed for a variety of species, methods for achieving the desired level of transgene expression in appropriate tissues are less well-established. With regard to transgenic animals, the introduction of DNA into the mammalian genome can ordinarily be achieved most reliably by microinjection or retrovirus-mediated gene transfer. However, the state of the art for transgenics and other *in vivo* genetic modifications is unpredictable because the method of gene transfer typically relies on random integration of the transgene construct or no integration. When random integration occurs, insertional inactivation of endogenous genes and position effects (see Wall, 1996, p. 61, paragraph 3) can dramatically influence the phenotype of the resultant genetically-modified animal. Integration of the transgene near highly active genes or, alternatively, in a transcriptionally inactive region, can influence its level of expression.

Furthermore, expression of the transgene and the effect of transgene expression on the phenotype of the genetically-modified animal depends on the particular gene construct used, to an unpredictable extent. The particular genetic elements required for appropriate expression varies from species to species. Thus, a construct that confers the desired phenotype in a rat cannot necessarily achieve the same result in a mouse. Wall (1996) reports that our lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior (p. 61, paragraph 3). This is especially relevant for species in which genetic studies are less advanced than in the mouse. Thus, the species-specific requirements for transgene design introduces an additional level of unpredictability associated with the development of genetically-modified animals. Even differences in the genetic background of transgenic mice can have an unpredictable effect on phenotype (Sigmund, 2000). In the absence of specific guidance, the production of a transgene-dependent phenotypic alteration resulting from the introduction of a nucleic acid construct as recited in the claim, is unpredictable. Thus, given the limited working examples directed exclusively to genetically-modified rats, and the post-filing results directed to genetically-modified mice, the existence of any phenotypic alteration, other than the one disclosed in the specification, resulting from the introduction of a gene encoding an aberrant form of tau, is highly unpredictable. Given the limited working examples and the unpredictability in the art, one of ordinary skill in the art would have been required to engage in undue experimentation in order to make and use the genetically-modified rats and mice over the full scope.

The species-specific requirements for transgene design are not clearly understood. Examples in the literature aptly demonstrate that even closely related species carrying the same transgene construct can exhibit widely varying phenotypes. For example, several animal models of human diseases have relied on transgenic rats when the development of mouse models was not feasible. Mullins et al. (1990) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse *Ren-2* renin transgene. Hammer et al. (1990) describe spontaneous inflammatory disease in inbred Fischer and

Lewis rats expressing human class I major histocompatibility allele HLA-B27 and human $\beta_2$-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice (Mullins et al., 1989; Taurog et al., 1988) expressing the same transgenes that successfully caused the desired symptoms in transgenic rats.

Houdebine (1994) discloses that in the field of transgenics, constructs must be designed case by case, without general rules, to obtain good expression of a transgene; e.g., specific promoters, presence or absence of introns, etc. (page 275, column 1, paragraph 1). Wall (1996) discloses the unpredictability of transgene behavior due to factors such as position effect and unidentified control elements, which may result in a lack of transgene expression or variable expression (paragraph bridging pages 61-62). Additionally, Kappel et al. (1992) disclose the existence of inherent cellular mechanisms that may alter the pattern of gene expression such as DNA imprinting, resulting from differential CpG methylation (page 549, column 2, paragraph 4). The level of skill in the art of *in vivo* genetic modification is such that one cannot predict whether a transgene that is expressed in a mouse will also be expressed efficiently in another animal. For example, Strojek and Wagner (1988) point out that a high degree of expression of a transgene in a mouse is often not predictive of high expression in other species, including pigs and rabbits, because, for example, the cis-acting elements may interact with different trans-acting factors in these other species (paragraph bridging pages 238-239). Furthermore, Wall (1996) explicitly teaches that transgene expression and the physiological consequences of transgene expression are not always accurately predicted in transgenic mouse studies (page 62, paragraph 1).

Given that specific phenotypic alterations cannot be predictably achieved by merely transferring a gene of interest into a rat or mouse, specific guidance must be provided to enable the instant invention over the full scope. The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. The claims cover the use of the genetically-modified rats and mice as a model for Alzheimer's Disease (AD), but the specification does

not enable this use because the complex phenotypic features of AD are not reproduced in the genetically-modified rats and mice. The claims also cover the use of genetically-modified rats and mice expressing an aberrant form of tau as a model for Huntington's Disease and Parkinson's Disease, but the specification does not enable this use for either animal species. In the absence of specific guidance for making and using genetically-modified rats and mice exhibiting an appropriate phenotype, undue experimentation would have been required to make and use the full scope of rats and mice and to practice the claimed methods over the full scope.

Accordingly, given the demonstrated lack of predictability in the art, the limited amount of direction given, the state of the prior art, the quantity of experimentation needed, and the limited applicable working examples, one of skill in the art would not be able to practice the claimed methods over the full scope or make and use the claimed compositions over the full scope without undue experimentation.

At page 9, paragraph 2 of the response, Applicants assert that the amendments to Claims 23, 30, and 34 obviate this rejection. However, since Claims 34 and 35 continue to cover animals of all kinds, including human beings, none of which are enabled by the instant specification for the reasons discussed above and in the previous Office Actions, the amendments do not obviate this rejection. Furthermore, since the method claims continue to cover the use of rats and mice that have (i) a wide variety of phenotypes not enable by the specification, (ii) a wide variety of tau isoforms and (iii) a wide variety of tau mutations, the amendments clearly do not obviate this rejection.

At page 9, paragraph 3 of the response, Applicants argue that Nacharaju et al. (1999) teaches several tau mutations other than the P301L mutation exemplified in the specificaton. However, neither Nacharaju nor the instant specification teach the phenotype of a rat or mouse genetically modified by somatic cell gene transfer. Thus, for the reasons detailed above and in the previous Office Actions, the specification fails to provide an enabling disclosure for the use of rats and mice comprising a gene

encoding a mutant form of tau, other than the mutant form of human tau comprising the P301L mutation (see the last sentence at the bottom of page 5 of the Office Action mailed 11/19/03). Thus, the claims remain broader than the indicated scope of enablement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-28 and 30-35 stand rejected and Claims 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34 and 35 are indefinite in their recitation of "at least one gene construct" within the same claim that recites "a gene encoding an aberrant tau protein in a vector construct." A broad limitation together with a narrow limitation that falls within the broad limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, Claims 34 and 35 recite the broad recitation "at least one gene construct," and the claims also recite "a gene encoding an aberrant tau protein in a vector construct" which is the narrower statement of the limitation.

Claims 34 and 35 are indefinite in their recitation of "said gene" because the term has ambiguous antecedent basis as the claim refers to both "at least one gene" and "a gene encoding an aberrant tau protein in a vector construct."

Claims 25, 35, and 39-41 are indefinite in their recitation of "P301L" because no reference sequence is provided and therefore it is unclear what numbering system is being used and which residue of tau is being referred to.

At page 10, paragraph 4 of the response, Applicants argue that the nomenclature "P301L" is standard in the field of neurodegenerative diseases. Applicants state that it is

> "shorthand for describing specific mis-sense mutations (where a mutation in a sequence of nucleotides in DNA changes the codon for the amino acids in the protein gene product). The 'P' refers to the amino acid proline, '301' refers to nucleotide number 301 from the 5-prime end of the tau DNA coding sequence, and 'L' refers to leucine. 'P301L' is shorthand for 'a mutation at position 301 causing leucine to be incorporated in tau instead of proline.'" (page 10, paragraph 4 of the response).

First, Applicants are advised that '301' does not refer to "nucleotide number 301 from the 5-prime end of the tau DNA coding sequence," but rather refers to amino acid position 301. Second, Applicants have missed the point of the rejection. The rejection states that the terminology is indefinite because "no reference sequence is provided." The claims cover a wide variety of tau isoforms, including the various isoforms present in rats, mice, and humans. Humans alone express at least **six tau isoforms.** In humans, only the longest isoform has a proline at amino acid residue 301. So what does "P301L" mean in the context of the other five isoforms that do not have a proline at amino acid residue 301? Mice express at least 3 tau isoforms. Likewise, the mouse tau isoforms do not have a proline at amino acid residue 301. The term "P301L mutation" does not make sense in the context of the vast majority of tau proteins covered by the claims.

Claims 30-33 and 40 are indefinite in their recitation of "a method for inducing behavioral changes" because the preamble implies that behavioral changes will occur, but in fact no particular behavioral changes are achieved. Thus, the preamble in in conflict with the body of the claim.

*Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) The invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent.

Claims 34 and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Gotz et al. (2001).

Claims 34 and 35 are directed to a composition comprising a gene encoding an aberrant tau protein in a vector construct.

Gotz et al. (2001) discloses a vector construct comprising a cDNA encoding the longest human brain tau isoform comprising the P301L mutaton inserted into a murine Thy1.2 genomic expression vector (p. 529, column 2, paragraph 3). Transgenic mice overexpressing human tau are also disclosed.

Thus, the claimed invention is disclosed in the prior art.

Claims 34 and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Lewis et al. (2000).

Claims 34 and 35 are directed to a composition comprising a gene encoding an aberrant tau protein in a vector construct.

Lewis et al. (2000) disclose a vector construct comprising a cDNA encoding human tau comprising the P301L mutation inserted into a MoPrP vector (p. 404, column 2, paragraphs 2 and 3). Transgenic mice expressing the mutant P301L tau protein are also disclosed.

Thus, the claimed invention is disclosed in the prior art.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Dianiece Jacobs, whose telephone number is (571) 272-0532.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER